UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,564	07/19/2001	Gunter Schmidt	P-0279469/20	1520

909 7590 08/22/2003

PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	10

DATE MAILED: 08/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,564	SCHMIDT ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 18-24* is/are pending in the application.

4a) Of the above claim(s) *3-8,19,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9-13,18,20 and 23* is/are rejected.

7)☒ Claim(s) *24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 1-13, 18-24 remain pending.

Applicants' election of Group III (claims 1, 2, 9-13, 18, 20, 23, 24, drawn to a method which does not require capping steps) is acknowledged, as are the elected species [(a) trypsin, (b) CN-Br, (c) avidin/biotin support (d) bonding occurs at the C-terminus].

Applicants have traversed the restriction by arguing that the difference between Groups III and IV is not sufficient to render these groups "preferably distinct". The meaning of the phrase "preferably distinct" is not made clear. It is agreed that the inventions of Groups III and IV are related. But it is maintained that these two groups are patentably distinct. If, in response to this Office action, applicants were to make an admission that Group III is obvious over Group IV and *vice versa*, such an admission would be taken into account in deciding whether to maintain the restriction requirement. However, in the absence of such, Groups III and IV are regarded as distinct. Nevertheless, in the event that the Group III claims are found allowable in their present form, or in modified form, it would be appropriate to revisit the matter of the restriction. In the event that applicants were willing to introduce whatever limitations into Group IV that had been introduced into Group III, the original justification for imposing the restriction might then be called into question. Similarly, in the event that one or more of the elected claims are determined to be allowable, it may become appropriate to revisit the matter of restriction as it applies to claims 21 and

22. The restriction is maintained at the present time.

Claims 3-8, 19, 21, 22 are withdrawn from consideration.

*

Claims 9-13, 18, 20 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependendent claim cannot depend from any other multiple dependent claim. See MPEP 608.01(n).

*

Claims 9-13, 18, 20 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 9-13, 18, 20 is dependent on a non-elected claim.

*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned

at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 2, 23 are rejected under 35 U.S.C. §103 as being unpatentable over Tarr (USP 5,824,556).

Tarr discloses a method of mass spectrometric analysis of a set of truncated peptides, where the set of truncated peptides is generated by sequentially cleaving off the N-terminal amino acid from a peptide. The reagent used is carbon disulfide.

Consider what is, and is not required by the claims. The first point is that claim 1 does not require that the indicated steps be carried out in the order listed. Claim 1 encompasses the possibility that a peptide chemist carries out various fragmentation reactions, and subsequently generates a series of samples, which samples are then given to a mass spectroscopist. Once the samples have been analyzed by mass spectrometry, claim 1 does not require that any further cleavage or fragmentation reaction be carried out. Second, claim 1 does not require that the "second cleavage agent" be different from the first. It is true that claim 1 requires that the "second cleavage agent" cleave at a site that is different from the site cleaved by the first agent, but as long as the sites are different, claim 1 does not preclude the possibility that the "second cleavage agent" is the same as the first. In the case of the Tarr ('556) invention, the cleavage agent cleaves at a different site each time. It is true that the "site" is the N-terminal amino acid, but the "site" is different each time in

two respects. First, the peptide used will not, in general be a homopolymer (although it *could* be), and therefore each amino acid will be different, or at least there will be 20 (genetically encoded) possibilities. Second, the "site" is different in each case, since the number of amino acids separating the cleavage site from the C-terminal amino acid will decrease each time the cleavage is undertaken.

Thus, the claims are rendered obvious.

*

Claims 1, 2, 9, 13, 18, 23 are rejected under 35 U.S.C. §103 as being unpatentable over Hutchens (USP 6,124,137).

Hutchens discloses (col 35, line 54-65) the following sequence:

(a) digesting a peptide with trypsin;

(b) analyzing by MS;

(c) digesting the peptide with carboxypeptidase Y; and

(d) analyzing by MS

Thus, the claims are rendered obvious.

*

Claims 1, 2, 9, 13, 18, 23 are rejected under 35 U.S.C. §103 as being unpatentable over Hutchens (USP 6,124,137).

Hutchens discloses (col 39, line 38 to col 40, line 21) the following sequence:

(a) digesting a glycopeptide with trypsin;

(b) analyzing by MS;

(c) digesting the glycopeptide with carbohydrate-cleaving enzymes thereby generating (col 40, line 14) "fragmented glycopeptides"; and

(d) analyzing by MS.

Thus, the claims are rendered obvious.

*

Claims 1, 2, 9, 13, 18, 23 are rejected under 35 U.S.C. §103 as being unpatentable over Laal (USP 6245331).

Laal discloses (col 42, lines 10-38) formation of peptide fragments using *alpha*-mannosidase, subtilisin, chymotrypsin and trypsin. The resulting peptide fragments were then analyzed using mass spectrometry.

Thus, the claims are rendered obvious.

*

Claims 1, 2, 18, 23 are rejected under 35 U.S.C. §103 as being unpatentable over Furuya (*Biochem. Biophys Res. Commun* **163**, 1100, 1989).

Furuya discloses digestion of EGF separately with each of the following proteases: chymotrypsin, thermolysin and trypsin. At least one fragment from each of the digests was analyzed by MS.

The requirements of the claims are met if two or more different proteases are separately applied to the original sample. It may be the case that the reasons Furuya had for using multiple proteases was not the same as that of applicants. What matters is that Furuya accomplished what the claims require, and this is in fact the case.

Thus, the claims are rendered obvious.

*

Claims 1, 2, 18, 23 are rejected under 35 U.S.C. §103 as being unpatentable over Korostensky (*Electrophoresis* **19**, 1993, 1998).

Korostensky discloses (page 1935, col 2, paragraph 2) a procedure in which the following steps are undertaken:

(i) a protein is cleaved with an endoprotease

(ii) the mixture from step (i) is cleaved with an exoprotease

(iii) the mixture from step (ii) is then subjected to MS analysis.

It might appear at first glance that this is a different invention than what is claimed. But on closer inspection, it is evident that there is "less than meets the eye" in claim 1. Consider what claim 1 recites. In simple terms, the following steps are recited:

(a) cleaving with a first agent

(b) isolating one peptide, or all of the peptides

(c) subjecting the peptide or peptides to MS analysis

(d) cleaving with a second agent

(e) isolating one peptide, or all of the peptides

(f) subjecting the peptide or peptides to MS analysis

However, the steps do not have to be taken in the recited order, and moreover, there is nothing to preclude the possibility that two or more steps can be undertaken simultaneously. Thus, for example, suppose that step (d) is undertaken before step (b). One then obtains the following sequence:

(a) cleaving with a first agent

(d) cleaving with a second agent

(b) isolating one peptide, or all of the peptides

(c) subjecting the peptide or peptides to MS analysis

(e) isolating one peptide, or all of the peptides

(f) subjecting the peptide or peptides to MS analysis

Next, consider the fact that the claims permit one to "isolate" **all** of the peptides produced in the hydrolysis. However, this is not really much of an isolation; claim 1 does not actually require that any specific component of the mixture be separated from any other

specific component. Accordingly, if a person subjects a peptide to a proteolytic digestion, or multiple digestions, one can say that he has "isolated" the mixture in the sense that the mixture (the product of the digestions) is still in the flask or vial in which the digestion was conducted. It is noted also that claim 1 recites (step (b)) that one or more fragments must be "isolated" in which the fragment comprises the C-terminus or N-terminus of the peptide from which it was fragmented. However, this will always be the case. Suppose that one has a peptide that consists of 20 amino acids; let this be represented using numbers as follows:

1-2-3-4-5-6-7-8-9-10-11-12-13-14-15-16-17-18-19-20 [A]

This is designated peptide "A". Suppose that a given protease cleaves between residues 11 and 12. The result will be two peptides as follows:

[B]	[C]
1-2-3-4-5-6-7-8-9-10-11	12-13-14-15-16-17-18-19-20

(These are designated peptides "B" and "C"). Clearly both of these peptides meet the requirement of "comprising the C-terminus or N-terminus of the peptide from which it was fragmented". Next, suppose that these two fragments are further cleaved, specifically between residues 5 and 6, and between residues 15 and 16. The result will be the

following:

[D]	[E]	[F]	[G]
1-2-3-4-5	6-7-8-9-10-11	12-13-14-15	16-17-18-19-20

(These are designated peptides "D" - "G")

Thus, peptide "D" comprises the N-terminus of peptide A, and of peptide B. Peptide "E" comprises the C-terminus of peptide "B". Peptide "F" comprises the N-terminus of peptide "C". Peptide "G" comprises the C-terminus of peptide "A" and of peptide "C". Thus, invariably, all peptide fragments will "comprise the C-terminus or N-terminus of the peptide from which it was fragmented".

To reiterate what was stated above, claim 1 encompasses the following set of steps, since the steps can be undertaken in any order:

(a) cleaving with a first agent

(d) cleaving with a second agent

(b) isolating one peptide, or all of the peptides

(c) subjecting the peptide or peptides to MS analysis

(e) isolating one peptide, or all of the peptides

(f) subjecting the peptide or peptides to MS analysis

Suppose next that steps (b) and (e) are combined, and further that instead of isolating just one peptide, **all** of the peptides are "isolated". The result is the following:

(a) cleaving with a first agent

(d) cleaving with a second agent

(b) isolating all of the peptides

(c) subjecting the peptide or peptides to MS analysis

(f) subjecting the peptide or peptides to MS analysis

Suppose next that steps (c) and (f) are combined. The result is the following:

(a) cleaving with a first agent

(d) cleaving with a second agent

(b) isolating all of the peptides

(c) subjecting the peptide or peptides to MS analysis

Thus, claim 1 encompasses a process that consists of, or comprises these four steps. Essentially this is what is taught by Korostensky. The reference may not explicitly recite that a mixture of peptides is isolated, but given that there is no specific component that has to be separated from any other specific component, the "isolation" step is implicit in the reference.

Thus, the claims are rendered obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1653